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Chronic Pancreatitis with Inflammatory Mass in the Pancreatic Head

Ulrich F. Wellner, Kim C. Honselmann, and Tobias Keck

Department of Surgery, University Medical Center Schleswig-Holstein, Campus Lübeck, Lübeck, Germany

Definition

Chronic pancreatitis can present with enlargement and mass-formation of the pancreatic head, mimicking virtually all symptoms of a malignant pancreatic head tumor and confronting the clinician with significant diagnostic and therapeutic challenges. This phenomenon has been termed the "inflammatory (pseudo) tumor" [1], "tumor-forming chronic pancreatitis" [2], and other. For the purpose of this article, we will use the term inflammatory pancreatic head mass (IPHM).

From a pathophysiological point of view, IPHM is thought to result from recurrent acute and chronic inflammation of the pancreatic parenchyma, but at the same time to perpetuate disease progression as a "pacemaker" by causing main pancreatic duct (MPD) obstruction leading to chronic ductal hypertension [3]. There is no generally accepted definition of IPHM, but the following criteria may be applied: presence of an abnormally enlarged pancreatic head, often accompanied by pancreatic calcifications, MPD dilatation, and irregularities and atrophy of the pancreatic parenchyma to the left of the mesentericoportal axis [4–6] (Figs 51.1 and 51.2).

Incidence

The concept of the IPHM as a pacemaker of chronic pancreatitis has been established by Beger et al. [3] and followed mainly by European surgeons. The incidence of IPHM in surgical patients is in the range of 85%; however, exact figures have rarely been reported in detail [5,7]. The average size of the pancreatic head has been shown to be significantly larger in a study comparing German (median 4.5 cm) and North American (median 2.6 cm) patients undergoing surgery for chronic pancreatitis [5]. The significance of this finding lies in the fact that it explains regional differences in operative procedures used to treat chronic pancreatitis; however, the underlying cause is not clear. Reasons might be a pattern of clinical transfer of the patient from the gastroenterologist to the surgeon, genetic differences, or different risk factors for the development of chronic pancreatitis.

Symptoms, Pathophysiology, and Clinical Problems

An IPHM can cause many clinical symptoms and complications, which in principle constitute the classical complications of chronic pancreatitis. Differential diagnosis and decision-making may be complicated as virtually all of these symptoms can also be caused by pancreatic head cancer.

One of the most frequently reported symptoms is pain [4,7]. Typically, the pain maximum is located to the epigastric area and may radiate to the flanks and back. In some cases, however, back pain may be the primary complaint. The pain can be episodic or continuous, with sudden exacerbations of variable frequency from daily to once in several months, often triggered by alcohol or food intake. Signs of acute pancreatitis like elevation of serum amylase or lipase and edematous swelling of the pancreatic head are often found associated with severe acute pain attacks, but may as well be missing, especially with longer duration of disease. In line with this, there is good evidence from histopathological and experimental studies that pancreatic pain is not only caused by acute inflammation but also from chronic neuropathy of visceral nerves in the pancreas [8]. Importantly about 50–90% of patients will not become pain-free even 10 years after disease onset [9].

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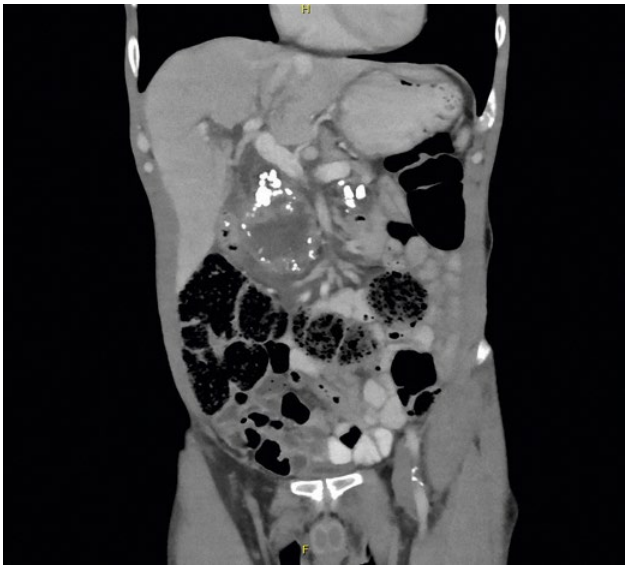

Figure 51.1 Inflammatory pancreatic head mass. Computed tomography showing a large inflammatory pancreatic head mass in a patient with chronic pancreatitis, with typical diffuse pancreatic calcifications and a large pseudocyst in the pancreatic head.

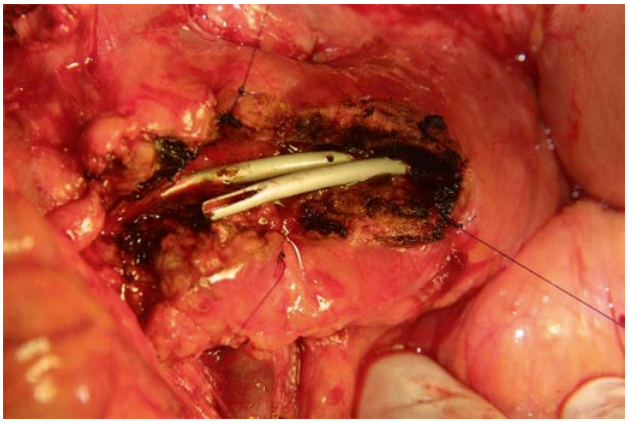

Figure 51.2 Impacted stent in the irregular and scarified main pancreatic duct. Prolonged interventional treatment leading to nonremovable stents in the pancreatic duct with marked pancreatic duct irregularities and narrowing.

Episodes of acute pancreatitis can lead to the development of pancreatic pseudocysts or walled-off necrosis (WON, Fig. 51.3) [10], with secondary complications like superinfection, pseudoaneurysm, hemorrhage, compression of the duodenum or bile duct, internal pancreatic fistula, and pancreatic ascites.

Biliary stricture is reported in up to 35% of patients [6], leading to jaundice and recurrent cholangitis. Of note, subclinical common bile duct (CBD) narrowing can be aggravated to frank obstruction by acute edematous swelling of the pancreatic head during episodes of acute

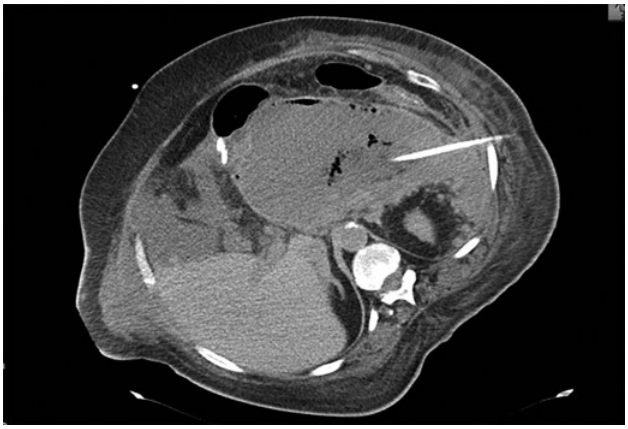

Figure 51.3 Walled-off necrosis. Magnetic resonance imaging depicting an inflammatory pancreatic head mass with walled-off necrosis which developed after an episode of acute pancreatitis in a patient with chronic pancreatitis. External interventional drainage.

pancreatitis. Maldigestion and absorption with steatorrhea, coagulopathy, and malnutrition occurs as a result of persistent cholestasis. Duodenal stenosis is found in about 10% of patients [6], resulting in gastric dilatation, postprandial bloating and vomiting, anorexia and malnutrition. Malnutrition may be exaggerated by pancreatic exocrine insufficiency. Loss of endocrine function typically occurs later and will affect around 80% of patients [9]. Stenosis and finally thrombotic occlusion of the mesentericoportal vessels is usually a late complication. Occlusion of the splenic vein results in left-sided portal hypertension with development of gastric fundal varices and splenomegaly. As complete occlusion of the portal vein usually develops gradually, extensive collaterals develop around the pancreatic head, a phenomenon called cavernous transformation [6]. Patients suffering from chronic pancreatitis have a 10-fold elevated risk of about 3% to develop pancreatic cancer [9].

Clinical Workup and Differential Diagnosis

The most important differential diagnoses are pancreatic head cancer and autoimmune pancreatitis. Careful clinical history-taking can yield important hints. Longstanding complaints or recurrent attacks over a period of years rather than months, accompanied by signs of chronic malnutrition points toward benign IPHM, whereas clinical deterioration over weeks to months with weight loss or new-onset diabetes mellitus are suggestive of malignancy. Jaundice can occur with IPHM but should always prompt efforts to rule out malignancy. Associated autoimmune disease points to autoimmune

pancreatitis [11]. Laboratory workup should include serum amylase and lipase activity and carbohydrate antigen 19-9 (CA19-9), as elevated serum enzyme activity indicates an episode of acute pancreatitis, whereas marked elevation of the tumor marker in absence of acute pancreatitis is suggestive of malignancy. Sensitivity and specificity of CA19-9 for discrimination of chronic pancreatitis from PDAC were reported as 84% and 75% [12]. Serum immunoglobulin G4 (IgG4) can be increased in autoimmune pancreatitis [13]. Because of the risk of tumor spillage and lack of therapeutic consequences, tissue biopsy is not recommended when resectable malignancy is suspected.

Cross-sectional imaging by contrast-enhanced computed tomography (CECT) or magnetic resonance imaging (MRI) is mandatory. In IPHM, the pancreatic head is enlarged with loss of the lobular parenchymal architecture, calcifications, and narrowing of the pancreatic duct (Fig. 51.1). There can be mass-forming lesions in the pancreatic head virtually indistinguishable from pancreatic cancer. Upstream MPD dilatation is often absent in autoimmune pancreatitis [11]. Accuracy of modern cross-sectional imaging for differentiation of IPHM and pancreatic cancer has been reported in the range of 90% [14]. Magnetic resonance cholangiopancreatography can be a valid substitute for invasive endoscopic retrograde cholangiopancreatography (ERCP) to assess configuration of the biliary tree and MPD (Fig. 51.2). In view of eventual surgical intervention, it is of paramount importance to assess mesentericoportal vein status and signs of portal hypertension.

Treatment

Asymptomatic IPHM virtually does not exist; however, symptom-free periods of weeks to months are common. Indications for invasive treatment are persistent pain or dependence on analgesics, recurrent acute pancreatitis, obstructive cholestasis, gastric outlet obstruction, development of persistent large or symptomatic pancreatic pseudocysts or walled-off pancreatic necrosis (WON), and suspicion of malignancy. Conservative management is chosen in case of inoperability or as a strategy to avoid operative treatment during a period of recovery, either after an episode of acute pancreatitis or as a bridge to operation.

Medical therapy consists of pain control and eventual substitution of pancreatic enzymes and insulin. It must be stressed that clinical remission of symptoms can be achieved by cessation of alcohol consumption in alcohol-induced chronic pancreatitis. Furthermore, the role of tobacco smoke as a causal agent has recently been recognized [15]. At least initially, surveillance of a pancreatic head mass by cross-sectional imaging should be performed every 3 to 6 months to rule out malignancy.

Endoscopic stenting of the MPD can be effective to induce remission of pancreatic cysts, pancreatic fistula as well as pain by decompression of the MPD. However, randomized trials have shown that surgical treatment provides more effective and durable pain control [16–18] and has been included in international guidelines [19,20]. For example, patients with obstructive chronic pancreatitis, who recently started opioid treatment (no longer than 6 months) were randomized to either early surgical drainage (by a lateral pancreaticojejunostomy or duodenum-preserving pancreatic head resection) or endoscopic drainage (stent, lithotripsy) within 6 weeks of randomization. Izbicki pain score [21] was significantly lower in patients treated with surgery than with endoscopic intervention [18]. In addition, the Izbicki pain score was found to be able to identify those patients who benefit most from surgery [21]. Another disadvantage of endoscopic therapy is the necessity of regular stent exchange every 3 to 6 months to prevent cholangitis and tissue overgrowth; however, while efficacy is similar between plastic stents and metal stents, reintervention is lower in fully covered self-expanding metal stents as shown in a recent randomized controlled trial for benign biliary strictures due to chronic pancreatitis [22]. When a stent cannot be removed due to incrustation or migration, surgical intervention is needed (Fig. 51.1). Stenting of the CBD for obstructive jaundice is only a short-term option as remission of CBD obstruction can only be expected in cases of acute edematous swelling of the IPHM in acute pancreatitis.

Operative therapy can be divided into drainage procedures and those procedures that involve resecting a part of the pancreas. While drainage procedures aim at decompression of the MPD by pancreatojejunostomy, removal of the IPHM is the goal of resectional procedures, which can be combined with MPD drainage. On surgical exploration, the IPHM is usually found to be heavily indurated, and the inflammatory fibrotic process may extend into the peripancreatic tissues causing heavy adhesions to the organs in vicinity, like the retropancreatic blood vessels, duodenum, and hepatoduodenal ligament. These conditions render operative procedures involving the pancreatic head very challenging and in rare cases even technically impossible, especially when associated mesentericoportal hypertension leads to diffuse bleeding.

Radical pancreatoduodenectomy (PD) with (Longmire-Traverso [23]) or without (Kausch-Whipple [24,25]) preservation of the pylorus is the procedure of choice when malignancy is suspected and offers very good long-term pain control in chronic pancreatitis. For the IPHM, duodenum-preserving pancreatic head resection (DPPHR) was developed by Beger and colleagues [3]. In the Frey modification [26], pancreatic parenchyma is spared by

excoriation of the IPHM without transsection at the pancreatic neck, and laterolateral pancreatojejunostomy ensures adequate MPD decompression. In the Hamburg modification of DPPHR [6], drainage of the MPD is further optimized by a V-shaped excision along the MPD. Randomized trials have shown reduced perioperative and short-term morbidity in DPPHR compared to PD with comparable long-term results [6]; however, long-term quality of life and serious adverse events after 24 months were equal between PD and DPPHR [27]. Equality in this context clearly speaks for duodenum-preserving procedures as organ preservation should be in the focus of every surgeon whenever possible. Equality was also reported for Beger versus Frey procedures [28,29] and so far no randomized trial has involved other DPPHR modifications.

Pure MPD drainage procedures like the Puestow-Gillesby [30] (pancreatic left resection with splenectomy and laterolateral pancreatojejunostomy), Partington-Rochelle [31] (laterolateral pancreatojejunostomy) or Izbicki [32] (longitudinal V-shaped excision and laterolateral pancreatojejunostomy) operations do not remove the IPHM. MPD drainage in unselected patients only achieved 50–65% permanent pain control [6], which is inferior to that of pancreatic head resection with 75–95% [33–45]. Although no randomized trial has compared drainage versus resection procedures, drainage procedures are therefore reserved for patients without IPHM.

However, in case of mesentericoportal vein occlusion with portal hypertension and cavernous transformation, pancreatic head resection becomes impossible and therapy is limited to operative or endoscopic MPD drainage. Preoperative recanalization of the portal vein can be performed in selected patients with short-segment portal vein occlusion [46]. Gastroenterostomy and hepaticojejunostomy are measures of last choice for biliary or duodenal obstruction.

Adequate timing is an important aspect in the management of patients with IPHM. Maximum duration of a trial of nonoperative management of IPHM should be 6 months, as optimal operative treatment usually becomes impossible in an advanced stage. In the presence of mesentericoportal vein narrowing or partial thrombosis, elective surgery should be performed as soon as possible, and prophylactic anticoagulation is advocated until surgery.

Certain contraindications impede early surgery. Cachexia should be treated by high-caloric nutrition with adequate simultaneous supplementation of pancreatic enzymes and vitamins, and in case of gastric outlet obstruction by jejunal tube feeding, to achieve adequate nutritional status for operation. Elective surgery is also not indicated before at least 3 months have passed since the last episode of acute pancreatitis. Serum pancreatic enzyme activity can be used to monitor acute pancreatitis activity.

On histopathological workup, IPHM is characterized by fibrotic atrophy of exocrine acinar epithelium, the remaining ductal and islet epithelia becoming "skeletonized" in fibrous connective tissue. Strong inflammatory granulocytic or lymphocytic infiltration is uncommon. In contrast, autoimmune pancreatitis typically shows duct-centric inflammation, with IgG4 positive plasma cells or granulocytic epithelial lesions [11]. As overall tissue organization is heavily disturbed and chronic pancreatitis can be associated with pancreatic intraepithelial neoplasia (PANIN), distinction from PDAC can be difficult even for experienced pathologists. Intraoperative frozen section examination at least of the surgical resection margins is mandatory and in case of any doubt, radical oncologic resection is warranted.

Summary

Chronic pancreatitis with inflammatory pancreatic head mass is a domain of surgical therapy. The main differential diagnoses are pancreatic head cancer and autoimmune pancreatitis. Best results are achieved by resection of the pancreatic head mass with adequate drainage of the pancreatic duct, but pancreatic head resection may become impossible in advanced stages of the disease. Adequate workup and timing of conservative and surgical therapy is of paramount importance for successful management.

References

1 Zech CJ, Bruns C, Reiser MF, Herrmann KA. [Tumor-like lesion of the pancreas in chronic pancreatitis: imaging characteristics of computed tomography]. Radiologe 2008;48(8):777–784.

2 Suda K, Takase M, Fukumura Y, Kashiwagi S. Pathology of autoimmune pancreatitis and tumor-forming pancreatitis. J Gastroenterol 2007;42(Suppl 18):22–27.

3 Beger HG, Krautzberger W, Bittner R, Buchler M, Limmer J. Duodenum-preserving resection of the head of the pancreas in patients with severe chronic pancreatitis. Surgery 1985;97(4):467–473.

4 Buchler MW, Martignoni ME, Friess H, Malfertheiner P. A proposal for a new clinical classification of chronic pancreatitis. BMC Gastroenterol 2009;9:93.

5 Keck T, Marjanovic G, Fernandez-del Castillo C et al. The inflammatory pancreatic head mass: significant differences in the anatomic pathology of German and American patients with chronic pancreatitis determine

very different surgical strategies. Ann Surg 2009;249(1):105–110.
6 Bachmann K, Izbicki JR, Yekebas EF. Chronic pancreatitis: modern surgical management. Langenbecks Arch Surg 2011;396(2):139–149.
7 van der Gaag NA, Boermeester MA, Gouma DJ. The inflammatory pancreatic head mass. Ann Surg 2009;250(2):352–353; author reply 353.
8 Demir IE, Tieftrunk E, Maak M, Friess H, Ceyhan GO. Pain mechanisms in chronic pancreatitis: of a master and his fire. Langenbecks Arch Surg 2011;396(2):151–160.
9 Lankisch PG, Lohr-Happe A, Otto J, Creutzfeldt W. Natural course in chronic pancreatitis. Pain, exocrine and endocrine pancreatic insufficiency and prognosis of the disease. Digestion 1993;54(3):148–155.
10 Banks PA, Bollen TL, Dervenis C et al., and Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62(1):102–111.
11 Frulloni L, Amodio A, Katsotourchi AM, Vantini I. A practical approach to the diagnosis of autoimmune pancreatitis. World J Gastroenterol 2011;17(16):2076–2079.
12 Talar-Wojnarowska R, Gasiorowska A, Olakowski M, Lekstan A, Lampe P, Malecka-Panas E. Clinical value of serum neopterin, tissue polypeptide-specific antigen and CA19-9 levels in differential diagnosis between pancreatic cancer and chronic pancreatitis. Pancreatology 2010;10(6):689–694.
13 Morselli-Labate AM, Pezzilli R. Usefulness of serum IgG4 in the diagnosis and follow up of autoimmune pancreatitis: a systematic literature review and meta-analysis. J Gastroenterol Hepatol 2009;24(1):15–36.
14 Mori H. New insight of pancreatic imaging: from "unexplored" to "explored". Abdom Imaging 2010;35(2):130–133.
15 Maisonneuve P, Lowenfels AB, Mullhaupt B et al. Cigarette smoking accelerates progression of alcoholic chronic pancreatitis. Gut 2005;54(4):510–514.
16 Cahen DL, Gouma DJ, Nio Y et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. N Engl J Med 2007;356(7):676–684.
17 Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. Endoscopy 2003;35(7):553–558.
18 Issa Y, Kempeneers MA, Bruno MJ et al., and Dutch Pancreatitis Study Group. Effect of early surgery vs endoscopy-first approach on pain in patients with chronic pancreatitis: the ESCAPE randomized clinical trial. JAMA 2020;323(3):237–247.
19 Beyer G, Habtezion A, Werner J, Lerch MM, Mayerle J. Chronic pancreatitis. Lancet 2020;396(10249):499–512.
20 Gardner TB, Adler DG, Forsmark CE, Sauer BG, Taylor JR, Whitcomb DC. ACG Clinical Guideline: chronic pancreatitis. Am J Gastroenterol 2020;115(3):322–339.
21 Bachmann K, Melling N, Groteluschen R et al. Morphologic factors predict pain relief following pancreatic head resection in chronic pancreatitis description of the chronic pancreatitis pain relief (CPPR) score. Ann Surg 2021;273(4):800–805.
22 Ramchandani M, Lakhtakia S, Costamagna G et al. Fully covered self-expanding metal stent vs multiple plastic stents to treat benign biliary strictures secondary to chronic pancreatitis: a multicenter randomized trial. Gastroenterology 2021;161(1):185–195.
23 Traverso LW, Longmire WP, Jr. Preservation of the pylorus in pancreaticoduodenectomy. Surg Gynecol Obstet 1978;146(6):959–962.
24 Kausch W. Das Carcinom der Papilla Duodeni und seine radikale Entfernung. Beitr Z Clin Chir 1912;78:439–486.
25 Whipple AO. A reminiscence: pancreaticduodenectomy. Rev Surg 1963;20:221–225.
26 Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. Pancreas 1987;2(6):701–707.
27 Diener MK, Huttner FJ, Kieser M et al., and ChroPac Trial Group. Partial pancreatoduodenectomy versus duodenum-preserving pancreatic head resection in chronic pancreatitis: the multicentre, randomised, controlled, double-blind ChroPac trial. Lancet 2017;390(10099):1027–1037.
28 Keck T, Wellner UF, Riediger H et al. Long-term outcome after 92 duodenum-preserving pancreatic head resections for chronic pancreatitis: comparison of Beger and Frey procedures. J Gastrointest Surg 2010;14(3):549–556.
29 Klaiber U, Alldinger I, Probst P et al. Duodenum-preserving pancreatic head resection: 10-year follow-up of a randomized controlled trial comparing the Beger procedure with the Berne modification. Surgery 2016;160(1):127–135.
30 Puestow CB, Gillesby WJ. Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. AMA Arch Surg 1958;76(6):898–907.
31 Partington PF, Rochelle RE. Modified Puestow procedure for retrograde drainage of the pancreatic duct. Ann Surg 1960;152:1037–1043.
32 Izbicki JR, Bloechle C, Broering DC, Kuechler T, Broelsch CE. Longitudinal V-shaped excision of the ventral pancreas for small duct disease in severe chronic pancreatitis: prospective evaluation of a new surgical procedure. Ann Surg 1998;227(2):213–219.
33 Adams DB, Ford MC, Anderson MC. Outcome after lateral pancreaticojejunostomy for chronic pancreatitis. Ann Surg 1994;219(5):481–487; discussion 487–9.
34 American Gastroenterological Association Medical Position Statement: treatment of pain in chronic pancreatitis. Gastroenterology 1998;115(3): 763–764.
35 Beger HG, Schlosser W, Friess HM, Buchler MW. Duodenum-preserving head resection in chronic pancreatitis changes the natural course of the disease:

a single-center 26-year experience. Ann Surg 1999;230(4):512–519; discussion 519–23.
36 Buchler MW, Friess H, Muller MW, Wheatley AM, Beger HG. Randomized trial of duodenum-preserving pancreatic head resection versus pylorus-preserving Whipple in chronic pancreatitis. Am J Surg 1995;169(1):65–9; discussion 69–70.
37 Delcore R, Rodriguez FJ, Thomas JH, Forster J, Hermreck AS. The role of pancreatojejunostomy in patients without dilated pancreatic ducts. Am J Surg 1994;168(6):598–601; discussion 601–2.
38 Greenlee HB, Prinz RA, Aranha GV. Long-term results of side-to-side pancreaticojejunostomy. World J Surg 1990;14(1):70–76.
39 Izbicki JR, Bloechle C, Knoefel WT et al. Complications of adjacent organs in chronic pancreatitis managed by duodenum-preserving resection of the head of the pancreas. Br J Surg 1994;81(9):1351–1355.
40 Jimenez RE, Fernandez-Del Castillo C, Rattner DW, Warshaw AL. Pylorus-preserving pancreaticoduodenectomy in the treatment of chronic pancreatitis. World J Surg 2003;27(11):1211–1216.
41 Riediger H, Adam U, Fischer E et al. Long-term outcome after resection for chronic pancreatitis in 224 patients. J Gastrointest Surg 2007;11(8):949–959; discussion 959–60.
42 Saeger HD, Schwall G, Trede M. [The Whipple partial duodenopancreatectomy--its value in the treatment of chronic pancreatitis]. Zentralbl Chir 1995;120(4):287–291.
43 Schnelldorfer T, Lewin DN, Adams DB. Operative management of chronic pancreatitis: longterm results in 372 patients. J Am Coll Surg 2007;204(5):1039–1045; discussion 1045–7.
44 Strate T, Taherpour Z, Bloechle C et al. Long-term follow-up of a randomized trial comparing the Beger and Frey procedures for patients suffering from chronic pancreatitis. Ann Surg 2005;241(4):591–598.
45 Wilson TG, Hollands MJ, Little JM. Pancreaticojejunostomy for chronic pancreatitis. Aust N Z J Surg 1992;62(2): 111–115.
46 Adam U, Makowiec F, Riediger H et al. Pancreatic head resection for chronic pancreatitis in patients with extrahepatic generalized portal hypertension. Surgery 2004;135(4):411–418.